Research Article / Araştırma Makalesi

Evaluation of Comorbidities, Laboratory Findings and Clinical Outcomes in Elderly Patients with COVID-19

COVID-19'lu Yaşlı Hastalarda Komorbidite, Laboratuvar Bulguları ve Klinik Sonuçların Değerlendirilmesi

Gökhan ÇAKIRCA[1], Tuba DAMAR ÇAKIRCA[2]

[1]Department of Biochemistry, Sanliurfa Mehmet Akif Inan Training and Research Hospital, Sanliurfa, TÜRKİYE
[2]Department of Infectious Diseases and Clinical Microbiology, Sanliurfa Training and Research Hospital, Sanliurfa, TÜRKİYE

Abstract

Background: In this study, we aimed to analyze the underlying diseases, laboratory findings and clinical outcomes of elderly patients infected with COVID-19. We also investigated the value of laboratory parameters in the estimation of critical cases and mortality in elderly patients.
Materials and Methods: The study included 314 elderly patients aged 60 years and older who were diagnosed with COVID-19.The patients were divided into two groups according to age, as young old patients (60-74 years) and old old patients (≥75 years). Participants' age, gender, underlying diseases, laboratory findings, disease severity and survival data were obtained from hospital records.
Results: The most common comorbidities in elderly patients were hypertension (57.6%), diabetes mellitus (33.8%) and cardiovascular disease (28%). Old old patients had higher rates of critical type (63.4% vs 30.8%, *P*<0.001) and death (41.9% vs 21.3%, *P*<0.001) compared to young old patients. The leukocyte count, neutrophil count, urea, creatinine, C-reactive protein (CRP), procalcitonin, ferritin, troponin T, creatine kinase-MB, prothrombin time and D-dimer values were higher in the old old group compared to the young old group. In contrast, hemoglobin and albumin values were lower in the old old group. The areas under the curve (AUC) of albumin, CRP, procalcitonin, ferritin, troponin T and prothrombin time were greater than 0.80 to predict critically elderly COVID-19 patients. Ferritin had the highest AUC for predicting death (AUC: 0.819) followed by CRP (AUC: 0.805) and procalcitonin (AUC: 0.796).
Conclusions: The rate of critical type and death were higher in old old patients compared to young old patients. In addition, ferritin, CRP, and procalcitonin were strong predictors of both disease severity and mortality in COVID-19-infected elderly subjects.

Key Words: COVID-19, Elderly patients, Clinical outcomes, Disease severity, Laboratory parameters

Öz

Amaç: Bu çalışmada COVID-19 ile enfekte yaşlı hastaların altta yatan hastalıklarını, laboratuvar bulgularını ve klinik sonuçlarını analiz etmeyi amaçladık. Ayrıca yaşlı hastalarda kritik vakaların ve mortalitenin tahmininde laboratuar parametrelerinin değerini araştırdık.
Materyal ve Metod: Çalışmaya COVID-19 teşhisi konan 60 yaş ve üzeri 314 yaşlı hasta dahil edildi. Çalışmaya dahil edilen hastalar yaşa göre genç yaşlı hasta (60-74 yaş) ve ileri yaşlı hasta (≥75 yaş) olmak üzere ikiye ayrıldı. Katılımcıların yaşı, cinsiyeti, altta yatan hastalıkları, laboratuar bulguları, hastalık şiddeti ve sağ kalım verileri hastane kayıtlarında elde edildi.
Bulgular: Yaşlı COVID-19 vakalarında en sık görülen komorbiditeler sırasıyla hipertansiyon (%57.6), diabetes mellitus (%33.8) ve kardiyovasküler hastalık (%28) idi. İleri yaşlı hastalarda, genç yaşlı hastalara kıyasla kritik tip (%63.4 vs %30.8, *P*<0.001) ve ölüm (%41.9 vs %21.3, *P*<0.001) oranları daha yüksekti. İleri yaşlı grubun lökosit sayısı, nötrofil sayısı, üre, kreatinin, C-reaktif protein (CRP), prokalsitonin, ferritin, troponin T, kreatin kinaz-MB, protrombin zamanı ve D-dimer değerleri genç yaşlı gruba göre daha yüksekti. Tam tersine, hemoglobin ve albümin değerleri ileri yaşlı grupta daha düşüktü. Kritik olan yaşlı COVID-19 hastalarını tahmin etmede albümin, CRP, prokalsitonin, ferritin, protrombin zamanı ve troponin T'nin ROC eğrisi altında kalan alanları (AUCs) 0.800'den büyüktü. Ferritin, ölümü öngörmede en yüksek AUC değerine sahipti (AUC: 0.819), ardından CRP (AUC: 0.805) ve prokalsitonin (AUC: 0.796) gelmekte idi.
Sonuç: İleri yaşlı hastalarda, genç yaşlı hastalara kıyasla hastalığın kritik tip oranı ve ölüm oranı daha yüksek idi. Ayrıca, ferritin, CRP ve prokalsitonin COVID-19 ile enfekte yaşlı bireylerde hem hastalık şiddetini hem de mortaliteyi öngörmede güçlü göstergeler idi.

Anahtar Kelimeler: COVID-19, Yaşlı hastalar, Klinik sonuçlar, Hastalık şiddeti, Laboratuvar parametreleri

Corresponding Author/Sorumlu Yazar

Dr. Gökhan ÇAKIRCA
Department of Biochemistry,
Sanliurfa Mehmet Akif Inan Training and Research Hospital,
Sanliurfa, TÜRKİYE

E-mail: cakirca.gokhan@gmail.com

Received / Geliş tarihi: 08.10.2022

Accepted / Kabul tarihi: 23.11.2022

DOI: 10.35440/hutfd.1186111

Introduction

The COVID-19 infection, which first started in Wuhan, China, has become a worldwide pandemic (1). Emerging evidence suggests that exaggerated immune response and hyperinflammation are linked to the pathophysiology of COVID-19 (2,3). An exaggerated inflammatory response resulting from the overproduction of proinflammatory cytokines along with chemokines by immune cells such as macrophages, natural killers, and lymphocytes following COVID-19 infection leads to a condition called cytokine storm or hypercytokinemia, which can cause acute respiratory distress syndrome, multiple organ failure, and finally death (4,5). Adverse outcomes, including death, have often occurred in patients with COVID-19 who are elderly and have underlying comorbidities due to their reduced immune function (6). Researchers have reported that advanced age is related to increased disease severity and death rate in COVID-19 (7,8). Therefore, in this paper, we focused on elderly patients infected with COVID-19 and analyzed their underlying diseases, laboratory findings and outcome data.

Materials and Methods

The current study included 314 elderly patients aged 60 years and older who were confirmed with COVID-19 in Şanlıurfa Training and Research Hospital between July and December 2020. Patients aged 60 years and older with negative SARS-CoV-2 PCR test were not included in the study. Patients were unvaccinated and and classic COVID-19 cases. The patients included in the study were divided into two groups according to age, as young old patients (60-74 years) and old old patients (≥75 years). Participants' age, gender, underlying diseases, laboratory results on admission and survival data were obtained from hospital records. In addition, all cases were classified as mild, moderate-severe, or critical based on disease severity (9). Biochemical parameters including urea, creatinine, albumin, aspartate transaminase

(AST), lactate dehydrogenase (LDH), ferritin, C-reactive protein (CRP), procalcitonin, D-dimer, troponin T and creatine kinase-MB (CK-MB) were analyzed on a Cobas 8000 analyzer (Roche, Germany).

Hemogram parameters were run on Sysmex XN-1000 analyzer (Sysmex, Japan), while coagulation parameters were determined with Sysmex CS-2000i analyzer (Sysmex, Japan).

Statistical analysis

Data were analyzed with SPSS (version 20.0) and P <0.05 was considered significant. Whether the variables were normally distributed or not was tested with the Kolmogorov-Smirnov test. Variables were evaluated using the Mann-Whitney U-test, Student's t-test, $\chi 2$ test, or Fisher's exact test, as appropriate, and results are given as median (min-max), mean ± SD or number (percentage).

The importance of laboratory parameters in the estimation of critical cases and deaths in elderly patients was determined by ROC analysis. The thresholds for interpreting the area under the curve (AUC) value were considered as: good (≥ 0.800), fair (0.700-0.799), and poor (<0.700) (10).

Results

This study enrolled 314 COVID-19-infected individuals, including the young old group (60-74 years; n= 221) and the old old group (≥75 years; n= 93). Of the patients, 142 (45.2%) were male and 172 (54.8%) were female. The most common underlying disease at admission was hypertension (57.6%), followed by diabetes (33.8%). The gender distribution and incidence of comorbidities (except for diabetes and dyslipidemia) were similar between the two groups.

Table 1. Characteristics of elderly patients with COVID-19

	All patients (n:314)	Young old (n: 221)	Old old (n:93)	*P*
Gender (male), n (%)	142 (45.2)	102 (46.2)	40 (43)	0.609
Past medical history, n (%)				
Hypertension	181 (57.6)	120 (54.3)	61 (65.6)	0.064
Diabetes mellitus	106 (33.8)	83 (37.6)	23 (24.7)	0.028
Cardiovascular disease	88 (28)	60 (27.1)	28 (30.1)	0.594
Dyslipidemia	84 (26.8)	67 (30.3)	17 (18.3)	0.028
Respiratory system disease	67 (21.3)	48 (21.7)	19 (20.4)	0.799
Cerebrovascular disease	18 (5.7)	11 (5.0)	7 (7.5)	0.375
Rheumatological diseases	6 (1.9)	5 (2.3)	1 (1.1)	0.674
Chronic renal failure	5 (1.6)	4 (1.8)	1 (1.1)	1.000
Chronic liver disease	4 (1.3)	1 (0.5)	3 (3.2)	0.080
Cancer	3 (1)	1 (0.5)	2 (2.2)	0.210
Clinical type, n (%)				
Mild	34 (10.8)	28 (12.7	6 (6.5)	
Moderate/severe	153 (48.7)	125 (56.5)	28 (30.1)	<0.001
Critical	127 (40.5)	68 (30.8)	59 (63.4)	
Outcomes, n (%)				
Discharge	228 (72.6)	174 (78.7)	54 (58.1)	<0.001
Death	86 (27.4)	47 (21.3)	39 (41.9)	

On the other hand, the frequency of diabetes and dyslipidemia was higher in the young-old group than in the old-old group. Classified according to disease severity, 48.7% of patients were moderate-severe, 40.5% were critical and 10.8% were mild. While most of the young old patients were moderate-severe type (56.5%), most of the old old patients were critical type (63.4%). The death rate in the old old group was 41.9%, significantly higher than in the young old group (Table 1).

Table 2 shows the laboratory results of the two groups. Leukocyte count, neutrophil count, urea, creatinine, CRP, procalcitonin, ferritin, troponin T, CK-MB, prothrombin time (PT) and D-dimer values of the old old group were higher than the young old group. On the contrary, hemoglobin and albumin values were lower in the old old group (P<0.05 for all).

As exhibited in Table 3, albumin, CRP, procalcitonin, ferritin, troponin T, and PT performed well in distinguishing elderly COVID-19 patients with or without critical as their areas under the curve (AUCs) were greater than 0.80. Ferritin, CRP, and procalcitonin AUC values for mortality in elderly COVID-19 patients were 0.819, 0.805, and 0.796, respectively (Table 4).

Table 2. Laboratory results of elderly patients with COVID-19

	Young (n)	Values	Old (n)	Values	*p*
Hemogram parameters					
Leukocyte, x10^3/µL	221	6.48 (1.30-31.06)	93	8.82 (2.92-27.14)	<0.001
Neutrophil, x10^3/µL	221	4.37 (0.99-27.75)	93	6.84 (1.57-25.21)	<0.001
Lymphocyte, x10^3/µL	221	1.31 (0.22-7.35)	93	1.30 (0.25-4.32)	0.481
Hemoglobin, g/Dl	221	13.2 ± 1.6	93	12.8 ± 1.7	0.041
Platelet, x10^3/µL	221	222 (73-659)	93	217 (53-575)	0.661
Biochemical parameters					
Urea, mg/dL	221	38.3 (13.2-249.2)	93	55.2 (20.4-286.8)	<0.001
Creatinine, mg/dL	221	1.02 (0.48-6.12)	93	1.18 (0.47-8.32)	0.011
Albumin, g/dL	219	4.0 (2.53-5.0)	92	3.6 (2.74-4.58)	<0.001
AST, U/L	221	32.2 (9.2-407.8)	93	32.6 (10.6-494.7)	0.996
LDH, U/L	217	307 (137-932)	90	331 (152-771)	0.107
CRP, mg/L	221	34.4 (0.6-408)	92	71.2 (0.6-336)	<0.001
Procalcitonin, ng/mL	217	0.08 (0.02-87.63)	93	0.17 (0.02-28.51)	<0.001
Ferritin, ug/L	161	343 (23-8037)	67	553 (40-4146)	0.007
Troponin T, ng/L	214	7(3-948)	88	20 (3-1980)	<0.001
CK-MB, ug/L	219	1.5 (0.3-41.5)	92	1.94 (0.3-28.7)	0.001
Coagulation parameters					
PT, s	220	11.8 (9.6-29.5)	92	12.8 (10.4-17.9)	<0.001
APTT, s	218	26.8 (18.6-56.7)	93	26.9 (19.7-46.3)	0.569
D-dimer, ug/mL	207	0.46 (0.15-9.11)	72	0.83 (0.15-11.69)	<0.001
Fibrinogen, mg/dL	168	76 (101-900)	79	414 (139-889)	0.243

AST: Aspartate transaminase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, CK-MB: Creatine kinase-MB, PT: Prothrombin time, APTT: activated partial thromboplastin time.

Table 3. The value of laboratory parameters in identifying critically ill older patients with COVID-19

	AUC (95% CI)	Optimal threshold	Sensitivity (%)	Specificity (%)	*P*
Leukocyte	0.760 (0.703-0.817)	7.48	74.0	73.3	<0.001
Neutrophil	0.788 (0.735-0.841)	5.48	74.0	76.5	<0.001
Lymphocyte	0.627 (0.563-0.692)	1.28	59.9	58.3	<0.001
Hemoglobin	0.525 (0.458-0.592)	13.2	-	-	0.448
Platelet	0.504 (0.436-0.572)	222	-	-	0.896
Urea	0.761 (0.705-0.817)	44.4	72.4	72.2	<0.001
Creatinine	0.693 (0.633-0.754)	1.08	63.8	63.6	<0.001
Albumin	0.825 (0.777-0.872)	3.81	77.2	77.2	<0.001
AST	0.672 (0.611-0.733)	33.4	63.8	64.2	<0.001
LDH	0.773 (0.719-0.828)	321	70.1	69.2	<0.001
CRP	0.821 (0.775-0.867)	50.6	74.0	75.3	<0.001
Procalcitonin	0.839 (0.791-0.886)	0.11	78.6	76.6	<0.001
Ferritin	0.805 (0.747-0.863)	402	72.9	72.7	<0.001
Troponin T	0.828 (0.779-0.878)	11.1	76.7	76.9	<0.001
CK-MB	0.643 (0.580-0.707)	1.72	60.3	60.0	<0.001
PT	0.805 (0.756-0.854)	12.2	74.0	73.5	<0.001
APTT	0.539 (0.471-0.608)	26.9	-	-	0.238
D-dimer	0.733 (0.669-0.797)	0.64	69.3	70.2	<0.001
Fibrinogen	0.607 (0.536-0.678)	456	57.5	55.9	0.004

AST: Aspartate transaminase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, CK-MB: Creatine kinase-MB, PT: Prothrombin time, APTT: activated partial thromboplastin time.

Table 4. Predictive powers of laboratory parameters for mortality in older COVID-19 patients

	AUC (95% CI)	Optimal threshold	Sensitivity (%)	Specificity (%)	*P*
Leukocyte	0.703 (0.635-0.771)	7.95	67.4	68.9	<0.001
Neutrophil	0.742 (0.680-0.804)	5.83	70.9	70.6	<0.001
Lymphocyte	0.654 (0.580-0.728)	1.23	61.8	62.8	<0.001
Hemoglobin	0.545 (0.466-0.624)	13.3	-	-	0.220
Platelet	0.536 (0.459-0.613)	215	-	-	0.325
Urea	0.707 (0.643-0.772)	47.0	66.3	66.2	<0.001
Creatinine	0.674 (0.607-0.741)	1.10	64.0	62.3	<0.001
Albumin	0.775 (0.719-0.830)	3.76	71.6	69.8	<0.001
AST	0.684 (0.620-0.748)	36.1	65.1	66.2	<0.001
LDH	0.768 (0.707-0.829)	348	72.1	72.6	<0.001
CRP	0.805 (0.755-0.855)	54.6	75.6	71.4	<0.001
Procalcitonin	0.796 (0.741-0.851)	0.15	75.3	79.1	<0.001
Ferritin	0.819 (0.764-0.874)	496	75.7	75.9	<0.001
Troponin T	0.757 (0.696-0.819)	11.8	72.8	71.9	<0.001
CK-MB	0.651 (0.583-0.719)	1.82	60.5	61.8	<0.001
PT	0.757 (0.701-0.813)	12.5	67.4	72.6	<0.001
APTT	0.603 (0.530-0.677)	26.9	60.5	54.7	0.005
D-dimer	0.669 (0.593-0.746)	0.66	65.2	64.3	<0.001
Fibrinogen	0.592 (0.518-0.667)	475	60.5	59.0	0.018

AST: Aspartate transaminase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, CK-MB: Creatine kinase-MB, PT: Prothrombin time, APTT: activated partial thromboplastin time.

Discussion

COVID-19 infection can cause serious complications (e.g., myocarditis, acute kidney injury, and thromboembolic events) and death (11). It has been reported that older age is an important predictor of mortality in previous coronavirus infections (SARS and MERS) (12,13). Similarly, advanced age has been shown to be correlated with increased morbidity and mortality in novel coronavirus infection (7,8). In a study by Dai et al. (14), it was revealed that elderly patients with COVID-19 have a higher rate of serious cases, complications and death compared to non-elderly patients. Moreover, Wei et al. (15) reported that oldest old people with COVID-19 had a higher rate of organ damage and mortality than younger old people with COVID-19. Our current study also confirmed that the disease was more severe and mortality was higher in old old COVID-19 patients compared to young old COVID-19 patients.

Researchers also reported that comorbidities are a risk factor for severe cases of COVID-19 and COVID mortality (14,16). Most of the elderly patients infected with COVID-19 in our study had one or more underlying diseases.The most common comorbidities in elderly patients were hypertension (57.6%), diabetes mellitus (33.8%) and cardiovascular disease (28%). The frequency of dyslipidemia and diabetes mellitus was slightly higher in the young old group compared to the old old group in our study. However, there was no difference between the two groups in terms of other comorbidities. Wei et al. (15) found the frequency of hypertension, coronary artery disease and cerebral infarction to be higher in old-old patients than in young-old patients. However, they found no difference in terms of other comorbidities. In another study, Guo et al. (17) found no difference in comorbidities between the two groups.

Looking at the laboratory findings, leukocyte count, neutrophil count and procalcitonin levels were higher in the old group than in the young old group, which indicates a higher probability of having a bacterial infection in these patients. Compared to the young-old group, the levels of kidney markers (urea and creatinine), cardiac markers (CK-MB and troponin T) and coagulation parameters (prothrombin time and D-dimer) were higher in the old-old group, reflecting that multiple organ damage was more pronounced in old old patients. In addition, the levels of inflammation markers (leukocyte, neutrophil, procalcitonin, CRP, and ferritin) were higher in old-old patients compared to the young-old group, which is evidence of a more severe course of COVID-19 disease in patients in this age group. Similar findings have been reported by other researchers (15, 17).

Malnutrition, which causes reduced immune system function, is frequent in patients with severe COVID-19 (18) due to many different factors including gastrointestinal symptoms such as diarrhea, vomiting and loss of appetite caused by COVID-19, which lead to reduced food intake; hypermetabolism and elevated energy expenditure (19); advanced age, underlying comorbidities and long-term intensive care unit stay (20). As is well known, albumin is a biochemical indicator that reflects nutritional status. Hypoalbuminemia in patients with COVID-19 may result from unsatisfactory intake, decreased production due to liver dysfunction caused by cytokine storm, increased loss from the kidneys, heavy consumption and enhanced capillary permeability (21,22). Previous reports have shown that low albumin levels are strongly associated with increased disease severity and reduced survival in COVID-19 patients (23,24). In the current study, we found lower albumin and hemoglobin levels in the old-old group compared to the young-old group. These results indicate that old old patients are in a poor nutritional state, which may cause increased severity of the disease.

Early diagnosis and treatment is of great importance for

COVID-19 infected elderly subjects (25). Laboratory parameters can help physicians assess the progression and prognosis of COVID-19, thereby improving disease management and minimizing mortality rates (26,27). Therefore, we also investigated the utility of routine laboratory parameters in predicting critical illness and death in elderly subjects infected with COVID-19. We found that albumin, CRP, procalcitonin, ferritin, troponin T and PT performed well in distinguishing between critically and non-critical elderly COVID-19 patients. On the other hand, performance of other parameters in predicting critically ill patients was fair or poor as AUC values were below 0.800. We also observed that ferritin, CRP and procalcitonin parameters were strong predictors of death in elderly COVID-19 patients, which were in line with the results of previous studies (25,28-30).

The main limitation of the study is its single-center and retrospective design. In addition, the clinical features, complications and treatment options of the patients were not analyzed due to the lack of data.

Conclusion

This study showed that critical cases and mortality rates were higher in the old-old group compared to the young-old group. In addition, ferritin, CRP and procalcitonin can be used as important indicators in the prediction of both disease severity and mortality in elderly subjects infected with COVID-19.

Acknowledgments

We thank Dr. Ayşe Torun (Department of Infectious Diseases and Clinical Microbiology, Sanliurfa Training and Research Hospital) and Dr. Reyhan Derya Portakal (Department of Chest Diseases, Sanliurfa Training and Research Hospital) for assistance in data acquisition.

Ethical Approval: *The study was approved by the Ethics Committee of Harran University (Date: 08/08/2022, No: HRÜ/22.15.07).*

Author Contributions:
Concept: G.Ç.
Literature Review: G.Ç., T.D.Ç.
Design : G.Ç.
Data acquisition: T.D.Ç.
Analysis and interpretation: G.Ç., T.D.Ç.
Writing manuscript: G.Ç., T.D.Ç.
Critical revision of manuscript: G.Ç., T.D.Ç.

Conflict of Interest: *The authors have no conflicts of interest to declare.*

Financial Disclosure: *Authors declared no financial support.*

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